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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,178	01/11/2002	Noriyuki Kasahara	06666-022002	7589

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EXAMINER
POPA, ILEANA

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,178	KASAHARA ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-46,49-51,56,58,59,61,63-73,75 and 77-86* is/are pending in the application.

4a) Of the above claim(s) *46 and 83-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-45,49-51,56,58,59,61,63-73,75 and 77-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

2. Claims 1-40, 47, 48, 52-55, 57, 60, 62, 74, and 76 have been cancelled. Claim 46 has been withdrawn. Claims 41, 58, 59, 66, and 80-82 have been amended. No new matter was introduced by these amendments.

Claims 83-86 are new. However, the newly submitted claims are directed to an invention that is distinct from the invention originally claimed for the following reasons: the invention originally claimed is drawn to therapy using suicide genes, whereas the new claims are drawn to therapy using cytokines

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 83-86 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 41-45, 49-51, 56, 58, 59, 61, 63-73, 75, and 77-82 are under examination.

Response to Arguments

Double Patenting

3. Claims 41-45, 49-51, 56, 58, 59, 61, 63-65, 80 and 81 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 20 of U.S. Patent No. 6,899, 871 because the Applicants did not submit a terminal disclaimer.

4. Claims 66-73, 75, 77-79 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 and 21 of U.S. Patent No. 6,899, 871 because the Applicants did not submit a terminal disclaimer.

5. Claim 82 remains rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19 of U.S. Patent No. 6,899, 871 because the Applicants did not submit a terminal disclaimer.

Claim Rejections - 35 USC § 112

6. Claims 41-45, 49-51, 56, 58, 59, 61, 63-73, 75, and 77-82 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons set forth in the prior Office Action. Applicant's arguments filed 07/28/2006 have been fully considered but they are not persuasive.

Applicants traversed the instant rejection on the grounds that the claimed invention is drawn to treating certain proliferative disorders using the retrovirus specified

in the claims and that the declaration of Dr. Noryuki Kasahara under 37 CFR 1.132 deascribes the manner in which one of skill in the art can use the method of the invention according to the disclosure of the present application and knowledge in the art to treat a cell proliferative disorder. Applicants argue that the declaration provides data indicating that the claimed method can be used to treat a cell proliferative disorder in animal models that are typically used in gene therapy research and that their vector is a replication competent vector that can achieve transduction and expression efficiencies never achieved by previous vectors. Applicants assert that the art of gene therapy is not unpredictable because one report (Crystal, Science, 1995, 270: 404) indicates that human gene transfer is feasible, that one of skill in the art could readily identify, without undue experimentation, the routes of administration and the therapeutic doses, and that their vector achieves transduction and expression efficiency never achieved by previous vectors. Regarding the fact that a tumor may develop resistance to the drug, Applicants assert that one of skill in the art would know how to select the proper prodrug-suicide gene combination for the claimed invention without undue experimentation, that treating a cell proliferative disorder does not require killing of all cells and that the partial alleviation of the symptoms of the disorder would be relieving and desirable by the subject to be treated. Applicants argue that, even if some cancer cells develop drug resistance, the method still treats the disorder by killing the drug-sensitive cells. Applicants claim that the specification provides a reasonable amount of guidance as to how to optimize the invention and therefore, no undue experimentation would be

necessary. In light of these arguments, Applicants request the withdrawal of the rejection.

Applicants' assertions have been considered but not found to be persuasive because of the specific reasoning as set forth in the prior Office Action. The assertions are simple conclusions without any evidential support, and thus, they are not sufficient to overcome the specific reasoning, doubts, and issues as set forth by the art of record. Contrary to Applicants assertion, the invention is not drawn to treating just certain proliferative disorders, the invention is drawn to the treatment of a very broad genus of disorders encompassing various neoplastic disorders and disorders associated with the overgrowth of connective tissue. The declaration under 37 CFR 1.132 filed 07/28/2006 has been considered fully to the extent that a tumor treatment of glioblastoma is disclosed with sufficient evidence to demonstrate the make and use of the claimed invention for tumor treatment in animal models, wherein a direct administration of the claimed retroviral vector to the tumor is employed. However, the breadth of the claims does not reflect what is shown in either the specification or the declaration. It is not apparent how treatment of tumors in animal models reasonably correlates with successful therapy, since the art clearly teaches that the validation of different approaches in animal models typically used in gene therapy research is not indicative of a therapeutic effect in human subjects. The art teaches that treatments effective in animal models are not effective in clinical trials, especially when the product is given alone (see Fillat et al.). The citation of Crystal has been considered fully by the Examiner, but the "potential usefulness" and "continues to be compelling" clearly show

that the specific issues set forth in the prior Office Action have not been overcome by the evidential support for the make and use of the claimed invention at the time the invention was made. Applicants assert that the art of gene therapy is not unpredictable because Crystal teaches that information gained from clinical trials indicate that human gene transfer is feasible. It is noted that Applicants' citation is taken out of the context and that Crystal clearly indicates that studies in experimental animals do not predict the efficacy of gene therapy in clinical trials. Overall the art teaches that efficacy in animal models does not correlate with efficacy in clinical trials. Regarding the Applicant' argument that their vector is a replication competent vector that can achieve high transduction and expression efficiencies, it is noted that the Applicants are not the first to discover the concept of making a replication competent retroviral vector. The make and use of replication competent vectors as simple gene transfer vectors were well known in the art at the time the invention was made. However, the art of record at the time the invention was made found that the use of retroviral vectors, routes of administration, gene expression at target sites, and the types of diseases remain complex and reasonably unpredictable (see Romano, cited in the prior Office Action). Regarding the argument that, even if some cancer cells develop drug resistance, the method still treats the disorder by killing the drug-sensitive cells, the art clearly teaches that cancer cells mutate rapidly and can readily adapt to most forms of therapeutic agents, i.e., the drug-sensitive cells rapidly acquire drug resistance as a response to their exposure to the drug, thus rendering the drug inefficient as a therapeutic agent (see Carbone et al. and Luqami, both cited in the prior Office Action).

In conclusion, one of skill in the art, who was (and still is) aware of the of the shortcomings and the doubts expressed by the art of record as a whole with respect to gene therapy protocols applied broadly to a number of neoplastic disorders or disorders associated with the overgrowth of the connective tissue, would not have readily accepted that Applicants' assertions together with the Declaration are sufficient to reasonable enable the claimed invention.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

JANET L. EPPS-FORD, PH.D.
PRIMARY EXAMINER